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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,224	12/09/2003	Neil P. Desai	225602	4904

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,224	DESAI ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,77-84 and 91-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6,9-11,18,77-83 and 91-96* is/are rejected.

7)☒ Claim(s) *4,7,8,12-17 and 84* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicants' remarks received June 16, 2005. Claims 19-76, 85-90 are canceled. Claims 94-96 are new. Claims 1-18, 77-84, 91-96 are pending and currently under examination.

Priority: The benefit date is December 9, 2002, for the purpose of prior art.

Withdrawal of Objections and Rejections

The rejection of claims 1-18, 77-84, 91-93 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn.

Maintenance of Objections and Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 is rejected again under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to a pharmaceutical agent selected from the group as disclosed in the claim and its derivatives. The claim recites a group of different

compounds that include small molecules, hormones, and a peptide, such as vasoactive intestinal peptide (VIP). It is known in the art that VIP is a 28-amino acid peptide. *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." As stated above, claim 3 is drawn to a numerous number of derivatives of any of the small molecules, hormones, or peptides listed in the claim. As an example using VIP, the skilled artisan cannot necessarily envision the detailed structures of ALL of the derivatives of vasoactive intestinal peptide that have functional activity the same as the wild-type VIP because nowhere in the specification is it described which amino acids are even essential and critical for the wild-type protein to maintain its functionality, and therefor conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of making the claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5, 18 are rejected again under 35 U.S.C. 102(b) as being anticipated by Yang et al. (Yang et al. 1993 Biochem. Pharm. 46(2) : 336-339). Yang et al. teach human serum was mixed with 4 vol. of Tris buffer and incubated with 5.5 μCi/mL of [^{3}H] dihydroartemisinin for 24 hr at 37° in the presence of deferoxamine (DFO, 1 mM) (p. 336; claims 1, 2, 5, 18). Yang et al. teach a mixture of human serum and Tris-HCl buffer (250 mM, pH 8.0) in a 1:4 v/v (p. 336). The composition of Yang et al., therefore meets the limitation of 25% by weight of albumin in claim 5. Yang et al. do not specifically teach the role or function of deferoxamine in the composition. However, the properties of inhibiting microbial growth (claim 1) and inhibiting oxidation (claim 18) are properties that are inherent to deferoxamine. It is known in the art that artemisinin is an effective anti-cancer agent (Singh et al. 2001 Life Sciences 70: 49-56).

In their response, Applicants assert the Yang et al. reference does not describe a pharmaceutical composition suitable for administration to a human, which will reduce side effects associated with administration. Applicants further assert there is no teaching to combine albumin, artemisinin and deferoxamine in a pharmaceutical composition or to use it as a treatment. The Examiner acknowledges Applicants remarks and will address the issues set forth by Applicants. As currently written, claims 1-2, 5, 18 are still drawn to a composition comprising a pharmaceutical agent and a pharmaceutically acceptable carrier. Statements of intended use or purpose are not

limiting to the interpretation. Therefore, as explained in the 35 U.S.C. 102(b) rejection above, Yang et al. teach a composition comprising albumin, deferoxamine, and artemisinin. The instant claims, minus claim 5, do not limit the amount of albumin, deferoxamine, and artemisinin that is present in the pharmaceutical composition, therefore, the Yang et al. reference is applicable and anticipate claims 1-2, 5, and 18.

Claims 1, 5-6, 9-11, 18 are rejected again under U.S.C. 102(b) as being anticipated by Ritov et al. (Ritov et al. 2001 Diabetes 50 : 1253-1262). Ritov et al. teach a medium comprising 100 mmol/l mannitol, 5.0 mg/ml bovine serum albumin (BSA), 100 umol/l deferoxamine mesylate, 20 umol/l leupeptin, etc. (p. 1254, preparation of homogenate; claims 1, 5-6, 9-11, 18). Ritov et al. teach a 5.0 mg/ml or 0.005 g/ml concentration of BSA (p. 1254). The weight/volume percent can often be used to calculate the percentage concentration. The volume of a solution in mL is very nearly numerically equal to the mass of the solution in grams (art of reference: Eggling). Therefore, the formuation of Ritov et al. comprises 0.5% of albumin by weight in a 1 ml volume of a composition (claims 5-6). The molar mass of deferoxamine mesylate is 656.79 g/mol (art of reference: drugs.com). Ritov et al. teach a 6.6×10^{-5} g/ml concentration of deferoxamine mesylate, that comprises 0.0066% by weight of deferoxamine myesylate in a 1 ml volume of the composition (claims 9-11). Though Ritov et al. do not specifically address the functions of inhibiting microbial growth (claim 1) and inhibiting oxidation (claim 18) in the composition, the limitations of claim 1 and

claim 18 are met because these are properties that are inherent to deferoxamine. It is known in the art that leupeptin can inhibit muscle degeneration.

Applicants assert the Ritov et al. reference does not disclose a pharmaceutical composition suitable for administration to a human. Applicants further assert Ritov et al. teach a preparation utilizing BSA, where it is known in the art that BSA is not acceptable for use in humans due to immunological reactions. The Examiner acknowledges Applicants' remarks. As currently written, claims 1, 5-6, 9-11, 18 are still drawn to a composition comprising a pharmaceutical agent and a pharmaceutically acceptable carrier. As explained with the Yang et al. reference above, statements of intended use or purpose are not limiting to the interpretation. Therefore, as explained in the 35 U.S.C. 102(b) rejection above, Ritov et al. teach a composition comprising albumin, deferoxamine, and artemisinin. In regards to Applicants' remark about utilizing BSA and the adverse immunological reactions that may arise when injected into humans, the Examiner acknowledges that this is possible and known in the art. However, as currently written, the instant claims do not limit albumin to a specific source of albumin, therefore the composition of Ritov et al. anticipates the instant claims as they are drawn to a composition comprising albumin, deferoxamine, and artemisinin.

Claims 77-83, 91-93 are rejected again under 35 U.S.C. 102(b) as being anticipated by Paal et al. (Paal et al. 2001 Eur. J. Biochem. 268: 2187-2191). In order to minimize vehicle-related toxicity, Paal et al. teach a novel, water-soluble formulation

in which paclitaxel is bound covalently to human serum albumin. Paclitaxel is a very potent antitumor agent. Paal et al. teach a sample preparation comprising of 3 μM albumin, 1% ethanol, and 0.5-150 μM paclitaxel (pH 6.5, 2.4 μM Cl^-) (p. 2188, sample preparation; claims 77-83, 91-93). The claims are drawn to a ratio of albumin to pharmaceutical agent at of 18:1 or less. The ratio of 3 μM albumin to 0.5 μM paclitaxel is 6:1. Even though this ratio is less than the ratios of 18:1, 12:1, and 9:1 of claims 80-82, respectively, it still meets the claim limitations.

Applicants assert Paal et al. teach a binding assay and not a pharmaceutical composition. Applicants further assert there is no teaching in Paal et al. of a pharmaceutical composition with an acceptable carrier in an amount effective to increase transport of a drug to a site of infirmity, as recited in instant claims 80-83. The Examiner acknowledges Applicants' remarks. As currently written, claims 77-83, 91-93 are still drawn to a composition comprising a pharmaceutical agent and a pharmaceutically acceptable carrier. As noted in the previous 35 U.S.C. 102(b) rejections above, statements of intended use or purpose are not limiting to the interpretation. Applicants' are correct their assertion that Paal et al. teach a binding assay. However, as a part of this assay, Paal et al. teach a formulation or composition comprising paclitaxel (an antitumor agent) and human serum albumin in a numerical ratio that meets the limitations of instant claims 77-83 and 91-93. The instant claims are broad enough such that they are anticipated by the Paal et al. reference.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 77-79, 91-93 are provisionally rejected again under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 10 of copending Application No. 10616709. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of copending Application No. 10616709 anticipate the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

As currently written, claims 77-79, 91-93 are drawn to a composition comprising albumin and a pharmaceutical agent, wherein the ratio of the albumin to pharmaceutical agent is about 18:1 or less. Therefore, the ratio can be any numerical value less than 18:1, including 0. In addition, the instant claims 77-79 and 91-93 are broad enough in nature such that the claims of copending Application No. 10616709 anticipate them.

New Objections and Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 94-96 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a pharmaceutical agent selected from the group as disclosed in the claims and its derivatives. The claims recite a group of different compounds that include small molecules, hormones, and a peptide, such as vasoactive intestinal peptide (VIP). It is known in the art that VIP is a 28-amino acid peptide. *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." As stated above, claims 94-96 are drawn to a numerous number of derivatives of any of the small molecules, hormones, or peptides listed in the claim. As an example using VIP, the skilled artisan cannot necessarily envision the detailed structures of ALL of the derivatives of vasoactive intestinal peptide that have functional

activity the same as the wild-type VIP because nowhere in the specification is it described which amino acids are even essential and critical for the wild-type protein to maintain its functionality, and therefor conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods of making the claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating or making it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Claims 4, 7-8, 12-17, 84 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 10, 2005

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER